THE CLAIMS

What is claimed is:

1. A co-extruded adverse agent particle comprising:
an extruded core comprising an adverse agent and a hydrophobic material; and
an extruded sheath comprising a hydrophobic material which at least partially surrounds the core.

2. The co-extruded adverse agent particle of claim 1, wherein the adverse agent is an opioid antagonist.

3. The co-extruded adverse agent particle of claim 1, wherein the sheath surrounds a majority of the outer surface of the core.

4. The co-extruded adverse agent particle of claim 3, wherein the core is substantially cylindrical and the sheath substantially surrounds the core in the radial direction along substantially the entire length of the core.

5. The co-extruded adverse agent particle of claim 4, wherein the adverse agent is an opioid antagonist; and the particle has a size of about 0.1 mm to about 3.0 mm in all dimensions.

6. The co-extruded adverse agent particle of claim 1, wherein the adverse agent is sequestered.

7. A dosage form comprising:
a plurality of first particles comprising an active agent; and
a plurality of co-extruded second particles comprising a core comprising an adverse agent and a sheath which at least partially surrounds the core.

8. The dosage form of claim 7, wherein the adverse agent is sequestered.

9. The dosage form of claim 8, wherein the adverse agent is present only in the core of the co-extruded second particles.

10. The dosage form of claim 8, wherein the active agent is an opioid agonist and the adverse agent is an opioid antagonist.

11. The dosage form of claim 10, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, desomorphine,

dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metophon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

12. The dosage form of claim 11, wherein the opioid agonist is selected from the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

13. The dosage form of claim 10, wherein the opioid antagonist is selected from the group consisting of cyclazocine, naloxone, naltrexone, nalmefene, nalbuphine, nalorphine, cyclazacine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

14. The dosage form of claim 13, wherein the opioid antagonist is selected from the group consisting of nalmefene, naloxone, naltrexone, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

15. The dosage form of claim 8, wherein the dosage form is an oral dosage form.

16. The dosage form of claim 8, wherein the dosage form comprises a capsule containing the first particles and the co-extruded second particles.

17. An oral dosage form comprising:

a plurality of first particles comprising an opioid agonist, wherein the first particles provide a controlled release of the opioid agonist upon oral administration to a patient; and

a plurality of co-extruded second particles comprising a core comprising an opioid antagonist and a sheath which at least partially surrounds the core.

18. The oral dosage form of claim 17, wherein the opioid antagonist is sequestered.

19. The oral dosage form of claim 18, wherein the sheath surrounds a majority of the core.

20. The oral dosage form of claim 19, wherein the first particles and the co-extruded second particles each have a size ranging from about 0.1 mm to about 3.0 mm in any dimension.

21. The oral dosage form of claim 20, wherein the core and the sheath of the co-extruded second particles each comprise at least one hydrophobic material.

22. The oral dosage form of claim 21, wherein the hydrophobic material is selected from the group consisting of acrylic and methacrylic acid polymers and copolymers, alkylcelluloses, natural and synthetic waxes, water insoluble waxes, fatty alcohols, fatty acids, hydrogenated fats, fatty acid esters, fatty acid glycerides, hydrocarbons, and hydrophobic and hydrophilic polymers having hydrocarbon backbones, and mixtures of any two or more of the foregoing.

23. The oral dosage form of claim 22, wherein the hydrophobic material comprises an ammonio methacrylate copolymer.

24. The oral dosage form of claim 22, wherein the opioid agonist is selected from the group consisting of alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, desomorphine, dextromoramide, dezocine, diampromide, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metophon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tramadol, tilidine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

25. The oral dosage form of claim 24, wherein the opioid agonist is selected from the group consisting of morphine, codeine, hydromorphone, hydrocodone, oxycodone, oxymorphone, dihydrocodeine, dihydromorphine, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

26. The oral dosage form of claim 22, wherein the opioid antagonist is selected from the group consisting of cyclazocine, naloxone, naltrexone, nalmefene, nalbuphine, nalorphine, cyclazacine, levallorphan, pharmaceutically acceptable salts thereof, and mixtures of any two or more of the foregoing.

27. The oral dosage form of claim 26, wherein the opioid antagonist is selected from the group consisting of naloxone, naltrexone and nalmefene, pharmaceutically acceptable salts thereof, any mixtures of any two or more of the foregoing.

28. The oral dosage form of claim 18, wherein the dosage form comprises a tablet comprising the first particles and the co-extruded second particles.

29. The oral dosage form of claim 18, wherein the dosage form comprises a capsule containing the first particles and the co-extruded second particles.

30. The oral dosage form of claim 18, wherein the co-extruded second particles release about 0.5 mg or less of the opioid antagonist *in vivo* following administration.

31. The oral dosage form of claim 30, wherein the co-extruded second particles release about 0.05 mg or less of the opioid antagonist *in vivo* following administration.

32. A method of making a plurality of adverse agent particles comprising:

co-extruding a core composition and a sheath composition to form an extrudate stand; wherein the sheath composition radially surrounds at least a majority of the core composition, the core composition comprises an adverse agent and a hydrophobic material, and the sheath composition comprises a hydrophobic material; and

cutting the extrudate strand at predetermined lengths to form a plurality of adverse agent particles.

33. The method of claim 32, wherein the adverse agent is an opioid antagonist; and the particles have a size of about 0.1 mm to about 3.0 mm in all dimensions.

34. The method of claim 32, wherein the adverse agent is sequestered.

35. A method of making a dosage form comprising:

(a) forming a plurality of first particles comprising an active agent;

(b) forming a plurality of second particles comprising an adverse agent by co-extruding a core composition and a sheath composition to form an extrudate strand; wherein the sheath composition radially surrounds a portion of the core composition, the core composition comprises the adverse agent and a hydrophobic material, and the sheath composition comprises a hydrophobic material; and cutting the extrudate strand at predetermined lengths to form a plurality of second particles; and

(c) adding the first particles and the second particles together in a form suitable for administration to a patient.

36. The method of claim 35, wherein the first particles and the second particles are substantially identical in appearance to each other.

37. The method of claim 36, wherein the active agent is an opioid agonist and the adverse agent is an opioid antagonist.

38. The method of claim 37, wherein the dosage form is an oral dosage form, and the first particles and the second particles each have a size of from about 0.1 mm to about 3.0 mm in all dimensions.

39. The method of claim 35, wherein the first particles and the second particles are placed into a capsule for administration to a patient.

40. The method of claim 35, wherein the adverse agent is sequestered.

41. A method for treating pain in a patient, said treatment comprising administering to said patient an oral dosage form comprising:

a plurality of first particles comprising an opioid agonist; and

a plurality of co-extruded second particles comprising a core comprising an opioid antagonist, and a sheath which at least partially surrounds the core.

42. The method of claim 41, wherein the adverse agent is sequestered.

43. The method of claim 41, wherein the opioid antagonist is present only in the core of the co-extruded second particles.

44. A method of reducing abuse, misuse or diversion of an oral dosage form useful for treating pain, comprising prescribing to a patient in need thereof the oral dosage form of claims 7 or 17.

45. A kit for treating pain in a patient, comprising:

a) at least one dose of an oral dosage form comprising:

a plurality of first particles comprising an opioid agonist; and

a plurality of co-extruded second particles comprising a core comprising an opioid antagonist and a sheath which at least partially surrounds the core; and

b) a printed set of instructions directing the use of the oral dosage form in an intact form to treat pain.

46. The kit of claim 45, wherein the opioid antagonist is sequestered.